

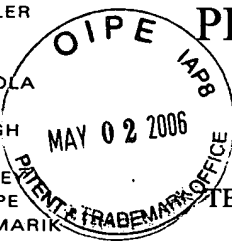
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April 26, 2006

SPE

Mail Stop Certificate of Corrections Branch  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Certificate

MAY 04 2006

of Correction

Re: U.S. Patent No.: 6,806,260  
Issued: October 19, 2004  
Inventor: Yura Hirofumi et al.  
Our Docket: 33550

Sir:

Applicant received notice from the U.S. Patent Office that request for correction to the above-identified patent was denied (copy of notice dated February 23, 2006 is enclosed). The notice stated that the subscript numbers in equations found in column 11, lines 1-26 and page 14 of the patent are blurred and too small to read. The notice stated that the reconsideration of the request for Certificate of Correction would be given if accompanied by supporting documents.

Enclosed is a second proposed Certificate of Correction for reconsideration, along with a clear copy of supporting documents taken from the specification as filed on August 13, 2001.

It is requested that the Certificate of Correction be completed and mailed at an early date to the undersigned attorney of record. The proposed corrections are obvious ones and do not in any way change the sense of the application.

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Mail Stop Decisions & Certificate of Corrections Branch, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on the date indicated below.

Amanda Wittine  
Name of Depositor

*Amanda Wittine*  
Signature of Depositor

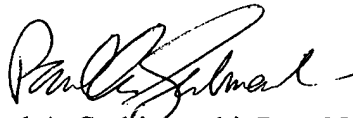
April 26, 2006  
Date

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U.S. Patent No.: 6,806,260  
Issued: October 19, 2004  
Atty. Docket No.: 33550  
Page 2 of 2

We understand that a check is not required since the errors were on the part of the Patent and Trademark Office in printing the patent.

Very truly yours,

A handwritten signature in black ink, appearing to read "Paul A. Serbinowski", with a horizontal line extending from the end of the signature.

Paul A. Serbinowski, Reg. No. 34429

PAS:alw  
Enclosures

MAY 09 2006

UNITED STATES PATENT AND TRADEMARK OFFICE  
CERTIFICATE OF CORRECTION

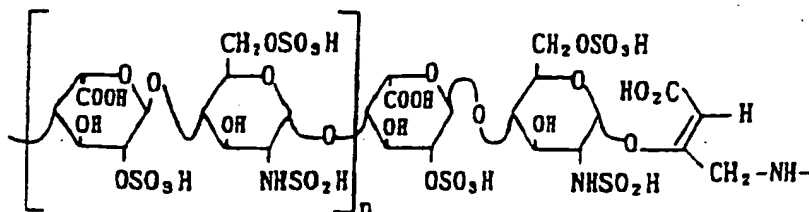
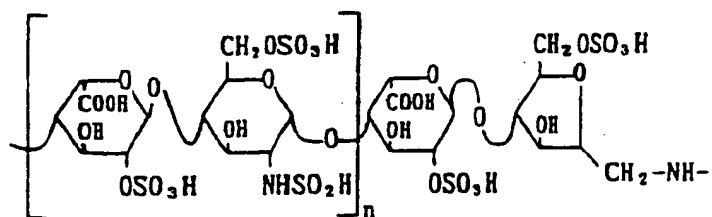
PATENT NO. : 6,806,260  
DATED : October 19, 2004  
INVENTOR(S) : Yura Hirofumi et al.

PAGE 1 OF 1

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

In Column 11:

Please delete the formulas found on lines 1-28, and insert the following therefor:



MAILING ADDRESS OF SENDER:

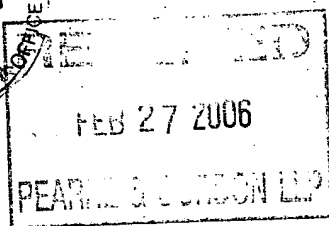
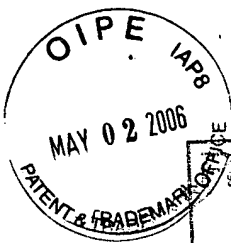
Paul A. Serbinowski  
Pearne & Gordon LLP  
1801 East 9th Street  
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PATENT NO. 6,806,260

No. of additional copies

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MAY 09 2006



WING  
UNITED STATES DEPARTMENT OF COMMERCE  
COMMISSIONER FOR PATENTS  
P.O. Box 1450  
Alexandria, VA 22313-1450

Date : 2/23/2006  
Patent No. : 6,806,260 B1  
Inventor(s) : Hirofumi et al.  
Issue Date : October 19, 2004  
Title : FUNCTIONAL CHITOSAN DERIVATIVE  
Doc./File No. : 33550

Re: Consideration for Certificate of Correction

Consideration has been given your request for the issuance of a certificate of correction for the above-identified patent under the provisions of Rule 1.322.

Respecting the alleged error(s) in your request, the subscript numbers in equations found in column 11, lines 1-26, and page 14 of the patent are blurred and are too small to read, please provide a clearer copy. No correction is in order here.

In view of the foregoing, your request for certificate of correction is hereby denied.

A certificate of correction will be issued to correct the remaining error(s) noted in your request.

Further consideration will be given concerning the matter of denials upon receipt of a request for **Reconsideration** (reconsideration should be accompanied by supporting document(s) such as, amendment, postcard receipt, 1449/892, etc.) and should be filed and directed to Decisions & Certificates of Correction Branch with the appropriate fee of 100.00, if necessary.

Ernest C. White, *LIE* (703) 308-9390 ext.#122  
Cecelia B. Newman, *Supervisor* (703) 308-9390 ext. #101  
Decisions & Certificates of Correction Branch

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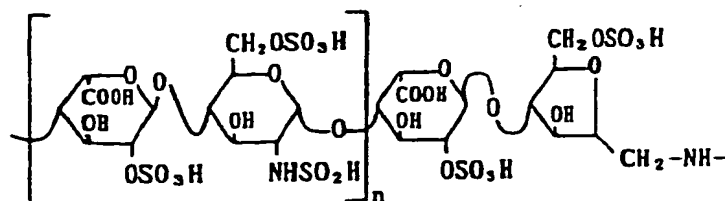
The healing promotion effect, in addition to wound repair, optimizes turnover of keratinocytes in the skin-care area, thus contributing to prevention of wrinkles.

While it has been suggested that chitosans naturally have a healing promotion effect, there have been reports that further healing promotion can be expected by ionic complexation of the glycosaminoglycans which are naturally-occurring acidic mucopolysaccharides with the basic groups of the chitosan (see Krats et al., *Sc and J Plat Reconstr Hand Surg*, 31, 119-123 (1997)). That is, the cell growth factors for stimulating the proliferation of fibroblasts and smooth muscle cells, which occurs during the healing process, are activated by binding to sulfated carbohydrates in the glycosaminoglycans.

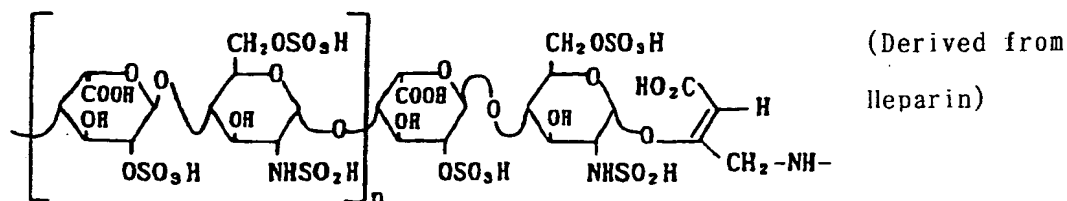
The incorporation of glycosaminoglycans to the chitosan of the present invention is not by the conventional ionic complexation method, and they are incorporated to the 2-position amino groups of the glucosamin unit of formula (1) by covalent bonds. The coupling method may, for example be the same method as the incorporation method for carbohydrates already explained, but in order to preserve sulfated carbohydrates to which cell growth factors can bind, it is possible to use a coupling method using aldehyde groups in which glycosaminoglycans are generated by means of periodic acid or nitrous acid decomposition.

Aside therefrom, coupling can be performed by binding through the above-mentioned chemical reaction to an insoluble self-crosslinked chitosan film due to photo-irradiation, or by binding by means of ionic complexation.

Specific examples of glycosaminoglycans incorporated in this way are those expressed by the following formulas, but there is no restriction to these.



(Derived from  
Heparin)



The degree of substitution of the glycosaminoglycans in the chitosan derivatives of the present invention is not particularly restricted, but should normally be within the range of 1-40%, preferably 10-30%.

In the chitosan derivative of the present invention, at least one substituent group can be appropriately chosen for incorporation from among a carbohydrate having a reducing terminal (first function), a photo-reactive functional group (second function), an amphipathic group (third function) and a glycosaminoglycan (fourth function) according to the intended use.

For example, by providing both a photo-reactive functional group and an amphipathic group, it is possible to obtain a chitosan derivative, which forms a hydrogel having both greater strength and water retaining ability. A chitosan derivative such as this would be a novel functional material capable of forming a chitosan having a certain degree of wound healing, adhesion prevention, humectants and anti-bacterial effects into an insoluble gel with a desired strength in a short period of time, which could be widely applied in the field of health care such as in medicine and cosmetics. In particular, chitosan derivatives incorporating carbohydrates excel in solubility in the neutral region, so that they may be made into solutions in biological buffer solutions or cultures. Furthermore, chitosan derivatives having photo-reactive functional groups form thick aqueous solutions at a concentration of 0.1 wt% or more, and after application to tissue, can be made to form an insoluble gel which adheres firmly with the tissue within a few minutes by irradiation by ultraviolet rays of a predetermined intensity. As a result, it can be freely coated on or implanted in burns, tissue deficient areas, surgical openings, cavities generated by losing teeth, bone deficient portions or the like, then irradiated for a short period of time to